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Disappointing Performance of Literature-Derived Selective Screening Criteria for Asymptomatic Chlamydia trachomatis *Infection in an Inner-City Population*

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Background: **In an inner-city population with a low prevalence of *Chlamydia trachomatis* infection, selective screening may be indicated to increase the efficiency of screening.**

Goal: **To evaluate the performance of sets of selective screening criteria for asymptomatic *Chlamydia trachomatis* infection in an inner-city population. The criteria were derived from reports of studies carried out in various settings.**

Study Design: **A total of 5714 women age 15 to 40 years living in Amsterdam were invited for a screening based on home-obtained urine specimens. Criteria identified from the literature were applied to the screening population. A calculated area under the receiver–operator characteristic curve (AUC) of greater than 0.75 was considered a good measure of diagnostic accuracy.**

Results: **Of the four sets of criteria, selection based on the following determinants showed the highest diagnostic accuracy: younger than 25 years, being unmarried, number of partners during the previous 6 months, Surinam or Antillean origin (black), and vaginal douching (AUC, 0.67; 95% CI, 0.65–0.69). Selection based on age alone showed an AUC of 0.57 (95% CI, 0.55–0.69).**

Conclusion: **The performance of selective screening criteria for asymptomatic *C trachomatis* infection in an inner-city population in Amsterdam was insufficient to recommend its implementation in practice.**

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A GENITAL *Chlamydia trachomatis* infection is the most prevalent sexually transmitted infection in industrialized countries. Untreated infections in women may lead to pelvic inflammatory disease, infertility, ectopic pregnancy, and chronic abdominal pain.[1] Scholes et al[2] demonstrated that the detection and treatment of asymptomatic *C trachomatis* infection in women leads to a reduced incidence of pelvic inflammatory disease.

The efficiency of screening depends on the prevalence of *C trachomatis* infection in the target population. In The Netherlands, screening is not routinely performed, and the prevalence of *C trachomatis* infections is relatively low.[3] A universal screening program may not be appropriate in a population with a low prevalence, but selective screening may be indicated.[4] Although various authors have proposed selective screening criteria for women, most of these criteria were derived from opportunistic or clinic-based screening programs, and may not be equally useful for screening in the general population.[5,6] Furthermore, these criteria have seldom been evaluated in a population other than that from which the criteria were derived, and reports of their performance may be too optimistic. The objective of this study was to evaluate the performance of literature-derived selective screening criteria for asymptomatic *C trachomatis* infection in a female inner-city population.

Methods

A random sample of 5714 women age 15 to 40 years was selected from the computer registers of 16 inner-city general practices in Amsterdam, The Netherlands. All women were invited to send in a home-obtained, first-void urine sample and to complete a questionnaire containing questions about demographic variables, current urogenital symptoms, history of sexually transmitted diseases, and sexual behavior. Patients were requested to return the urine specimen and the questionnaire to the laboratory of the Department of Pathology of the University Hospital Vrije Universiteit in a prestamped addressed envelope.

Urine samples were tested for the presence of *C trachomatis* DNA using ligase chain reaction (LCR; Abbott Laboratories, Chicago, IL). Tests were performed according to the instructions of the manufacturer.[7–9]

The test results were reported to the practice in which the

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TABLE 1. Performance of Four Sets of Selective Screening Criteria for Asymptomatic *Chlamydia trachomatis* Infections, Identified From the Literature, in an Inner-City Population

Set	Criteria*	Reference	Setting	AUC (95% CI)	Cutoff† (predicted probability)	Sensitivity‡ (%)	% Total Population Screened§	Prevalence in Screened Population‖
1	Age (y)	6,10,13	Military, FP, PC	0.57 (0.55–0.59)	Age ≤ 34 y	79.0	73.4	3.0
2	Age ≤ 25 y, ≥ two partners in the previous 6 months or new partner in the previous 2 months[¶#]	4,5,12	GP, FP/STD, PC	0.60 (0.58–0.62)	> 2.3%	46.2	29.5	4.6
3	Age ≤ 25 y, inconsistent condom use, ≥ two partners in the previous 6 months or new partner in the previous 2 months, history of STI	10	Military	0.60 (0.58–0.62)	> 2.3%	73.7	64.9	3.4
4	Unmarried, age ≤ 25 y, nulligravidity, ≥ two partners in the previous 6 months, Surinam/Antillean origin, vaginal douching	2/11	HMO/PC	0.67 (0.65–0.69)	> 3.2%	80.8	59.9	3.9

*Determinants from this study were chosen to match criteria recommended in studies from the literature as closely as possible (e.g., Surinam/Antillean origin is mainly "black").
†Cutoff at which the sensitivity of the criteria is 80%. All cases with a predicted probability above the cutoff would be selected for screening.
‡For comparability, a cutoff was chosen at a sensitivity as close as possible to 80%.
§True positive fraction + false positive fraction.
‖Positive predictive value.
¶Information regarding symptoms among partners not available.[8]
#Information regarding pregnancy not available.[2,7,9]
AUC = area under the receiver–operator curve; FP = family planning clinic; PC = primary care clinic; STD = sexually transmitted disease clinic; STI = sexually transmitted infection; HMO = health maintenance organization.

patient was registered, and practitioners were instructed to treat infected patients with a single 1000-mg dose of azithromycin (or for pregnant women, four 500-mg doses of erythromycin for 5 days) and to notify their partners.

At the end of the study, a nonparticipant study was also carried out. Every practice was requested to supply information regarding age, marital status, type of health insurance, and ethnic origin for 50 randomly chosen nonparticipants. Moreover, practitioners were requested to check whether the address listed in the computer register at the start of the study was correct.

Selection of Criteria From Other Studies

A MEDLINE search was performed to identify all reports of studies published between 1980 and 1998 evaluating and recommending selective screening criteria for asymptomatic *C trachomatis* infection in women. All sets of criteria that were based on determinants obtained during a physical examination were excluded (Table 1).

Statistical Analysis

Logistic regression analyses were performed with the sets of criteria identified from the literature using the SPSS version 7.5.2 (SPSS Inc., Chicago, IL). Subsequently, the probability of having a *C trachomatis* infection was calculated using the following formula:

$$p(C\ trachomatis) = \frac{1}{e^{-(a+B_1*x_1+\ldots B_k*x_k)}}$$

Where $P(C\ trachomatis)$ is the probability of infection, a is the constant, and B represents the regression coefficient for every determinant or interaction term x. Using the predicted probabilities a receiver–operator characteristic (ROC) curve, a plot of the sensitivity against 1−specificity, was calculated using Medcalc version 4.20.021 (F. Schoonjans, Belgium). The calculated area under the ROC curve (AUC) is a measure of the diagnostic accuracy, or the chance of correctly classifying a randomly selected couple of positive–negative observations, regardless of the cut-off value for positivity. Before analyzing the data, it was decided that an AUC of less than 0.60 was poor, an AUC of 0.60 to 0.75 was moderate, and an AUC of greater than 0.75 was good.

To ensure the identification of a sufficient number of cases should the program be implemented, a cut-off point was chosen for each model at which the calculated sensitivity was close to 80%. The sensitivity of the criteria, the percentage of the total population selected for screening (true-positive fraction + false-positive fraction), and the prevalence in the screened population (positive predictive value) were calculated at this cut-off point.

Results

The participation rate among the women who had been invited was 51%. Forty-one samples and questionnaires were excluded from the analysis, either because the respon-

TABLE 2. Characteristics of Participants and Nonparticipants in a Screening Program for Asymptomatic *Chlamydia trachomatis* Infections by Means of Mailed, Home-Obtained Urine Specimens

Characteristic	Prevalence of Characteristic (%)		
	Nonparticipants (n = 216)	Participants* (n = 2,060)	
Age (y)			NS
15–20	12.1	7.9	
21–25	13.1	17.3	
26–30	25.2	28.2	
31–35	30.8	25.7	
36–40	18.7	20.9	
Origin			$P < 0.001$†
Dutch	59.3	76.5	
Other European	5.3	3.4	
Surinam/Antillean	13.9	11.3	
Turkish/Moroccan	11.0	4.0	
Other	10.5	4.8	
Married or cohabiting			NS
Yes	51.7	49.1	
No	48.3	50.9	
Type of health insurance			NS
Government	75.0	75.0	
Private	25.0	25.0	

*Participants from practices that supplied information on nonparticipants.
†Chi-square test.

dent was not included in the study sample or because insufficient urine had been provided.

The questionnaire concerning nonparticipants was completed by 12 of the 16 practices. Other practices were unwilling to supply additional information about women who had indirectly declined to participate in the study by not returning the questionnaire or sample.

After the study commenced, it was found that 15% of the nonparticipants no longer lived at the address listed in the computer register at the start of the study. Participants were more frequently of Dutch origin than nonparticipants (Table 2). Age, marital status, and type of health insurance were similar in both groups. The prevalence of asymptomatic *C trachomatis* infection in women was 2.8% (95% CI, 2.2–3.4); 125 women had never been sexually active and were therefore excluded from further analysis.

Seven studies evaluating one or more sets of screening criteria for asymptomatic infections were identified. Four different sets of criteria were derived from these studies. Most of these criteria had been developed in populations of women attending primary care or family planning practices, one set was developed in a military population, and one set had been applied to a health maintenance organization population.

Table 1 shows the performance of the four sets of selective screening criteria identified from the literature in the inner-city population with a low prevalence of *C trachomatis* infection. Selection based on age alone showed the lowest diagnostic accuracy (AUC, 0.57; 95% CI, 0.55–0.59). Selection based on the determinants of an age of younger than 25 years, being unmarried, number of partners during the previous 6 months, Surinam or Antillean origin (black), and vaginal douching showed the highest diagnostic accuracy (AUC, 0.67; 95% CI, 0.65–0.69). Application of these criteria identified a subgroup of women with a prevalence of 3.9%.

Discussion

Selective screening criteria for asymptomatic *C trachomatis* infection among women that were identified from the literature were applied to a general population sample. Studies identified from the literature reported unanimously that efficient selection for screening was possible, yet the performance of most of the criteria in the current study population was poor (AUC < 0.75) (Table 1). The set with the best diagnostic accuracy included the determinants of being unmarried, younger than 25 years of age, having two or more partners in the previous 6 months, Surinam or Antillean origin (black), and vaginal douching (AUC, 0.67; 95% CI, 0.65—0.69). Data regarding parity and current pregnancy were not available in this study. Although these determinants were included in the original set of selection criteria or were used as an inclusion criterion for the study, it is thought that this did not significantly influence the results.

Several factors may have contributed to the poor performance of the selection criteria in this study. First, most criteria were derived from screening programs for women attending clinics. This study reports on systematic screening in a general population sample. The association between determinants and the risk of *C trachomatis* infection could be very different in both populations and settings. Opportunistic clinic-based studies generally report higher prevalences and a stronger association with age than population-based studies.

Second, the poor performance could be due to potential selective participation. Participants were compared to nonparticipants on several demographic variables, and participants were similar to nonparticipants regarding marital status, type of health insurance, and age. However, participants were more likely than nonparticipants to be of Dutch origin (Table 2). This difference may be due to cultural or language barriers, though information about the study was provided in the four most relevant languages in Amsterdam. There is no available information regarding other determinants of infection among nonparticipants (e.g., sexual risk behavior).

Third, most criteria were identified in studies carried out in the United States. There may be differences in sexual behavior (risk determinants) between various countries, particularly between The Netherlands and the United States.

Finally, the operationalization of determinants varies between studies, and respondents may interpret the questions

in a different manner. One example is the determinant of multiple partners within a certain period. In some studies, this determinant was defined as two or more partners in the past year, and in others the period included the past 3 months. In the current study, the period was 6 months; however, only small differences result from these time variations. Moreover, self-reported data regarding sexual behavior may not always be reliable, and may result in the misclassification of respondents.

Although some sets of criteria slightly increased the efficiency of detecting asymptomatic *C trachomatis* infection, the diagnostic accuracy found in the inner-city population sample was insufficient to recommend the implementation of any of the sets of criteria identified from the literature.

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